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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/623,611	10/06/2000	Maria Galanis	674537-2002	3929
20999	7590	08/19/2005	EXAMINER	
FROMMER LAWRENCE & HAUG 745 FIFTH AVENUE- 10TH FL. NEW YORK, NY 10151			OUSPENSKI, ILIA I	
			ART UNIT	PAPER NUMBER
			1644	

DATE MAILED: 08/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/623,611

Applicant(s)

GALANIS ET AL.

Examiner

ILIA OUSPENSKI

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06/22/2005.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2,4-9,12-21,28,34,35 and 38 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 14-17 is/are allowed.
- 6) ☒ Claim(s) 2,4-9,12,13,18-21,28,34,35 and 38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

5-0-0

DETAILED ACTION

1. Applicant's amendment/remarks, filed 06/22/2005, is acknowledged.

Claim 41 has been cancelled.

Claims 1, 3, 10, 11, 22 – 27, 29 – 33, 36 – 37, and 39 – 41 have been cancelled previously.

Claims 2, 4 – 6, 13, and 15 have been amended.

Claims 2, 4 – 9, 12 – 21, 28, 34, 35, and 38 are pending.

2. This Office Action will be in response to applicant's arguments, filed 06/22/2005.

The rejections of record can be found in the previous Office Action, mailed 03/22/2005.

The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.

3. Claim rejection under **35 USC 112, second paragraph**: Applicant's amendment has obviated the rejection of record.

4. Claim rejection under **35 USC 102(b) over Peach et al.**:

Claims 2, 7 – 9, 12 – 13, 20 – 21, 28, 34, 35, and 38 stand rejected under 35 U.S.C. 102(b) as being anticipated by Peach et al. (of record; J. Exp. Med., 1994, 180: 2049 – 2058; see entire document), essentially for the reasons of record.

Applicant's arguments have been fully considered but have not been found convincing.

Applicant argues that Peach et al. do not teach increasing the size of the CDR loop structure by any number of amino acids, and points to page 2052, Figure 3 and Table 2 of the reference for support.

This is not found persuasive, because Peach et al. teach replacement of homologous regions between CD28 and CTLA-4, where such regions are not equal in length. For example, in creating ligand HS3, as compared to either HS2 or HS4 (Figure 3), in the region between conserved cysteines at positions 21 and 94 the CTLA-4 sequence has been replaced with the corresponding CD28 sequence, which is longer by one amino acid, as evidenced by the alignment in Figure 1. Therefore, such replacement amounts to increasing the size of the CDR loop structure by one amino acid. (It is noted that absent an explicit definition of the term "CDR loop structure" in the instant specification, the broadest reasonable interpretation is assumed to encompass at least a structure comprising a CDR loop, e.g. the V-like domain of CD28 or CTLA-4).

Therefore, the rejection of record is maintained for the reasons of record, as it applies to the amended claims. The rejection of record is incorporated by reference herein, as if reiterated in full.

5. Claim rejection under **35 USC 103(a)** over **Peach et al.** in view of **Bogden et al.** and over **Peach et al.** in view of **Cai et al.**: The rejections of record have been withdrawn in view of Applicant's amendments and arguments.

6. Claim rejection under **35 USC 103(a)** over **Peach et al.** in view of **Koide**:

Claims 2, 4 – 6, and 18 – 19 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Peach et al. (of record; J. Exp. Med., 1994, 180: 2049 – 2058; see entire document) in view of Koide (of record; US Pat. Pub. No. 2003/0134386; see entire document).

Applicant's arguments have been fully considered but have not been found convincing.

Applicant argues that fibronectin type III (Fn3) domain taught by Koide is different from the V-like domain of the present invention. This is not found persuasive, at least in view of the following passage from paragraph 0097: "The structure [of Fn3 domain] is best described as a beta-sandwich similar to that of Ab VH domain except that Fn3 has seven beta-strands instead of nine (FIG. 1). There are three loops on each end of Fn3; the positions of the BC, DE and FG loops approximately correspond to those of CDR 1, 2 and 3 of the VH domain, respectively (FIG. 1 C, D)" (underlining added). Therefore, Koide teaches that in spite of the different number of beta strands between the Fn3 domain and the antibody VH domain, their structure is sufficiently similar to allow for meaningful correspondence with the CDR regions.

Applicant further argues that while Koide claims loop insertions up to 25 amino acids, it appears unlikely that a loop of this length would be functional in inserted into Fn3. This is not found persuasive in the absence of supporting evidence.

Applicant further argues that while Koide mentions that loops of the Fn3 domain can be replaced with loop structures derived from antibodies, no functional data has been provided, and therefore the teachings of Koide are not enabling for the present invention. This is not found persuasive in the absence of any evidence that the invention of Koide cannot function as taught.

Applicant further argues that Koide does not teach labeling of VLD molecules, and cites paragraph 135 which discloses that complexes of Fn-based "monobodies" ("FnAbs") with protein G should be labeled for use in NMR studies. This is not found persuasive because the paragraph teaches that "the small size, the high stability and solubility of both components and the ability to label each with stable isotopes (^{13}C and ^{15}N ; see below for protein G) make the complexes an ideal model system for NMR studies on protein-protein interactions" (underlining added). Therefore, Koide clearly teaches labeling the Fn-based binding ligands.

Applicant further argues that Koide teaches that complexes of Fn-based ligands rather than the ligands themselves are ideal models for studies of protein-protein interactions and therefore, the skilled artisan would have no reasonable expectation of success in producing a binding ligand. The relevance of this argument is not clear. It appears that if a skilled artisan has an expectation of success in producing a complex, he/she would expect to be equally successful in first producing its constituent components.

Finally, Applicant argues that Peach et al. teach away from the present invention, because their hybrid molecules did not fully restore wild-type CTLA-4-Ig binding activity. Here, Applicant is arguing limitations which are not claimed, because the instant claim language does not require the claimed molecule to have a specific binding activity.

Therefore, the rejection of record is maintained for the reasons of record, as it applies to the amended claims. The rejection of record is incorporated by reference herein, as if reiterated in full.

7. Conclusion: claims 14 – 17 appear to be allowable.

Art Unit: 1644

8. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILIA OUSPENSKI whose telephone number is 571-272-2920. The examiner can normally be reached on Monday-Friday 9 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ILIA OUSPENSKI
Patent Examiner
Art Unit 1644
August 15, 2005


PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
TECH CONTROL 1600
8/17/05